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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/412,539 10/04/99 KUCERA

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009629
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HM22/1031

EXAMINER

COLEMAN, B

ART UNIT

PAPER NUMBER

1624

DATE MAILED:

10/31/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.
09/412,539

Applicant(s)
KUCERA et al.

Examiner
Brenda Coleman

Art Unit
1624



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on Aug 27, 2001
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 56-71, 95, 96, and 101 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 56-71, 95, 96, and 101 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- *See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) ☐ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
- 18) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other: _____

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DETAILED ACTION

Claims 56-71, 95, 96 and 101 are pending in the application.

This action is in response to applicants' amendment filed August 27, 2001.

Response to Arguments

Applicant's arguments filed August 27, 2001 have been fully considered with the following effect:

1. With regards to the 35 U.S.C. § 112, second paragraph rejections labeled d) and f) maintained in the last office action, the applicants' remarks have been fully considered but they are not found persuasive.

d) The applicants' stated that "one of ordinary skill in the art would understand that where a substituent is not clearly indicated on an atom which is a member of a ring and which has capacity for an additional covalent bond, a hydrogen atom would normally be present" and "one of skill in the art *also* understands that a hydrogen atom would not be present when another substituent or an additional covalent bond takes the place of the hydrogen". The applicants' use benzene as an example to assert that one of ordinary skill in the art would know that a hydrogen atom would be assumed where no atom or variable is depicted. That convention is only in place for carbon not for nitrogen. Formula VII does not indicate that there is a hydrogen atom or a substituent attached to the nitrogen atom of position 3 nor does it indicate that there is the presence of an optional double bond between

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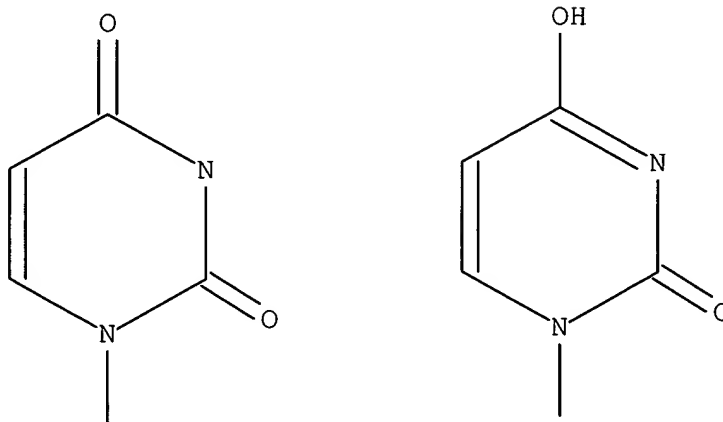
positions 3 and 4. The applicants' further stated that in the specification at page 12, lines 23-27 that "those skilled in the art will appreciate that the double bonds illustrated in Formula VII are included therein to represent that the moieties have aromatic character, *and* that these double bonds may shift for certain substituents, in particular for =O and NH₂ at positions 2 and 4, in order for the moiety to retain its aromatic character". However, Formula VII only illustrates the one double bond between positions 5 and 6, thus the "double bonds **illustrated**" only pertains to the double bond between positions 5 and 6 and the double bond of the =O at the 2 position.

Claims 56-71, 95, 96 and 101 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. For reasons of record and stated above.

- f) The applicants' stated that "the specification (as well as claim 56) contemplates the presence of a double bond between the 3 and 4 positions on the pyrimidinyl moiety generally described as Formula VII". The applicants' further stated that in the specification at page 12, lines 23-27 that "cytosine's double bond is merely shifted relative to Formula VII, in order for the moiety to retain its aromatic character". However, applicants' are asserting that Formula VII contains a double bond between positions 3 and 4 which does not result in a shift for cytosine because the

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double bond in cytosine is in positions 3 and 4. For there to be a double bond shift there first must be a double bond such as the one in the substituent =O of position 4, i.e.



Assuming a H atom on the N of position 3

However, cytosine has NH_2 at the 4 position. Without the double bond there can be no bond shift.

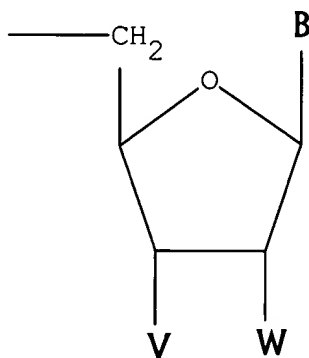
Claim 68 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. For reasons of record and stated above.

2. With regards to the 35 U.S.C. § 112, first paragraph rejection of claim 101, the applicants' remarks concerning the enablement of "tumor" is acknowledged but not found persuasive. The applicants stated that "one of skill in the art can make and use the invention without undue

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experimentation". The applicants' also stated that they "have found that the compounds of the invention have anti-cancer activity (see, e.g., page 15, lines 9-11) and have disclosed in the specification manners of carrying out the method of the invention to treat cancers". The applicants have pointed to *In re Wands* which discusses "a number of factors to determine whether a disclosure was sufficient to enable one of ordinary skill in the art to practice the invention throughout its scope without having to engage in undue experimentation". The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

The nature of the invention in the instant case, has claims which embrace **ionic** compounds as shown by Formula III. The instant compounds of Formula III are such that the Z substituent is



which is not described in the disclosure in such a way the one of ordinary skill in the art would not know how to prepare the various compounds suggested by claim 101. For example where are the starting materials for the preparation of these ionic compounds. There is not one working example

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provided in the specification for the preparation of the ionic compounds as claimed herein. Thus, in view of the lack of direction provided in the specification regarding starting materials, the lack of working examples, and the general unpredictability of chemical reactions, it would take an undue amount of experimentation for one skilled in the art to make the claimed compounds and therefore practice the invention.

HOW TO USE: Claim 101 is to "a method of combating tumors in a subject in need of such treatment comprising administering....a compound.....of Formula III". Any evidence presented must be commensurate in scope with the claims and must clearly demonstrate the effectiveness of the claimed compounds. However, the specification provides no definitive evidence to correlate that any tumor would be combated with the instantly claimed ionic compounds.

No screening protocol(s) are ever described. Thus, no evidence of in vitro effectiveness is seen in the specification for one of the instantly claimed ionic compounds. In general, pharmacological activity is a very unpredictable area. In cases involving physiological activity "the scope of the enablement obviously varies inversely with the degree of unpredictability of the factors involved." *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970). Since this case involves unpredictable *in-vivo* physiological activities, the scope of the enablement given in the disclosure presented here was found to be low.

The specification does not have working examples on the use of the ionic compounds of Formula III. The absence of working examples is one of the factors to be considered in deciding

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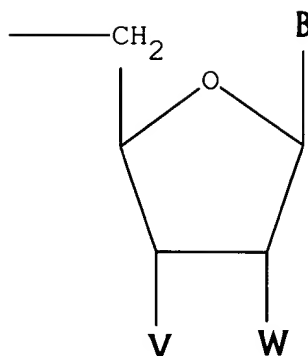
whether the practice of an invention would involve undue experimentation. There must be evidence to justify the contention that the claimed compounds can be useful in the treatment of tumors.

Claim 101 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. For reasons of record and stated above.

3. With regards to the 35 U.S.C. § 112, first paragraph rejection of claims 56-71 and 96, the applicants' remarks concerning the enablement of "viruses" is acknowledged but not found persuasive. The applicants stated that "an agent which inhibits viral replication or infection will have usefulness in treating viruses". The applicants have pointed to *In re Wands* which discusses "a number of factors to determine whether a disclosure was sufficient to enable one of ordinary skill in the art to practice the invention throughout its scope without having to engage in undue experimentation". The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

The nature of the invention in the instant case, has claims which embrace **ionic** compounds as shown by Formula III. The instant compounds of Formula III are such that the Z substituent is

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which is not described in the disclosure in such a way the one of ordinary skill in the art would not know how to prepare the various compounds suggested by claim 101. For example where are the starting materials for the preparation of these ionic compounds. There is not one working example provided in the specification for the preparation of the ionic compounds as claimed herein. Thus, in view of the lack of direction provided in the specification regarding starting materials, the lack of working examples, and the general unpredictability of chemical reactions, it would take an undue amount of experimentation for one skilled in the art to make the claimed compounds and therefore practice the invention.

HOW TO USE: Claim 101 is to "a method of combating a viral infection in a subject in need of such treatment comprising administering....a compound....of Formula III". Any evidence presented must be commensurate in scope with the claims and must clearly demonstrate the effectiveness of the claimed compounds. However, the specification provides no definitive evidence to correlate that any tumor would be combated with the instantly claimed ionic compounds.

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No screening protocol(s) are ever described. Thus, no evidence of in vitro effectiveness is seen in the specification for one of the instantly claimed ionic compounds. In general, pharmacological activity is a very unpredictable area. In cases involving physiological activity "the scope of the enablement obviously varies inversely with the degree of unpredictability of the factors involved." *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970). Since this case involves unpredictable *in-vivo* physiological activities, the scope of the enablement given in the disclosure presented here was found to be low.

The specification does not have working examples on the use of the ionic compounds of Formula III. The absence of working examples is one of the factors to be considered in deciding whether the practice of an invention would involve undue experimentation. There must be evidence to justify the contention that the claimed compounds can be useful in the treatment of viral infections.

Claims 56-71 and 96 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. For reasons of record and stated above.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).


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A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brenda Coleman whose telephone number is (703) 305-1880. The examiner can normally be reached on Mondays and Tuesdays from 9:00 AM to 3:00 PM and from 5:30 PM to 7:30 PM and on Wednesday thru Friday from 9:00 AM to 6:00 PM.

The fax phone number for this Group is (703) 308-4734 for "unofficial" purposes and the actual number for **OFFICIAL** business is **308-4556**.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.


Brenda Coleman
Primary Examiner AU 1624
October 30, 2001